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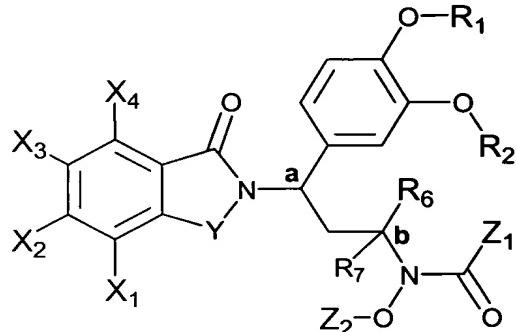
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**WHAT IS CLAIMED IS:**

1. A compound of formula (I):



5 wherein:

Y is -C(O)-, -CH<sub>2</sub>- or -CH<sub>2</sub>C(O)-;

R<sub>1</sub> and R<sub>2</sub> are each independently C<sub>1-8</sub>-alkyl, CF<sub>2</sub>H, CF<sub>3</sub>, CH<sub>2</sub>CHF<sub>2</sub>, cycloalkyl, or (C<sub>1-8</sub>-alkyl)cycloalkyl;

Z<sub>1</sub> is H, C<sub>1-6</sub>-alkyl, NH<sub>2</sub>, NR<sub>3</sub>R<sub>4</sub> or OR<sub>5</sub>;

10 Z<sub>2</sub> is H or C(O)R<sub>5</sub>;

X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub> and X<sub>4</sub> are each independently H, halogen, NO<sub>2</sub>, OR<sub>3</sub>, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl, (C<sub>0-4</sub>-alkyl)-(C<sub>3-6</sub>-cycloalkyl), (C<sub>0-4</sub>-alkyl)-N-(R<sub>8</sub>R<sub>9</sub>), (C<sub>0-4</sub>-alkyl)-NHC(O)-(R<sub>8</sub>), (C<sub>0-4</sub>-alkyl)-NHC(O)CH(R<sub>8</sub>)(R<sub>9</sub>), (C<sub>0-4</sub>-alkyl)-NHC(O)N(R<sub>8</sub>R<sub>9</sub>), (C<sub>0-4</sub>-alkyl)-NHC(O)O(R<sub>8</sub>), (C<sub>0-4</sub>-alkyl)-O-R<sub>8</sub>, (C<sub>0-4</sub>-alkyl)-imidazolyl, (C<sub>0-4</sub>-alkyl)-pyrrolyl, (C<sub>0-4</sub>-alkyl)-oxadiazolyl, (C<sub>0-4</sub>-alkyl)-triazolyl or (C<sub>0-4</sub>-alkyl)-heterocycle;

R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> are each independently H, C<sub>1-6</sub>-alkyl, O-C<sub>1-6</sub>-alkyl, phenyl, benzyl, or aryl;

R<sub>6</sub> and R<sub>7</sub> are independently H or C<sub>1-6</sub>-alkyl;

R<sub>8</sub> and R<sub>9</sub> are each independently H, C<sub>1-9</sub>-alkyl, C<sub>3-6</sub>-cycloalkyl, (C<sub>1-6</sub>-alkyl)-(C<sub>3-6</sub>-

20 cycloalkyl), (C<sub>0-6</sub>-alkyl)-N(R<sub>4</sub>R<sub>5</sub>), (C<sub>1-6</sub>-alkyl)-OR<sub>5</sub>, phenyl, benzyl, aryl, piperidinyl, piperizinyl, pyrrolidinyl, morpholino, or C<sub>3-7</sub>-heterocycloalkyl; or a pharmaceutically acceptable salt or solvate thereof.

2. The compound of claim 1 wherein Y is -CH<sub>2</sub>- or -C(O)-.

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3. The compound of claim 1 wherein Z<sub>1</sub> is H.

4. The compound of claim 3 wherein R<sub>6</sub> is C<sub>1-6</sub>-alkyl and R<sub>7</sub> is H.
5. The compound of claim 1 wherein Z<sub>2</sub> is H, -C(O)CH<sub>3</sub> or -C(O)CH<sub>2</sub>CH<sub>3</sub>.
- 5
6. The compound of claim 5 wherein X<sub>4</sub> is NHC(O)R<sub>8</sub>.
7. The compound of claim 5 wherein R<sub>1</sub> is CH<sub>3</sub> or CF<sub>2</sub>H and R<sub>2</sub> is C<sub>1-8</sub>-alkyl.
- 10
8. The compound of claim 5 wherein Z<sub>2</sub> is H.
9. The compound of claim 1 wherein R<sub>1</sub> is CH<sub>3</sub> or CF<sub>2</sub>H.
- 15
10. The compound of claim 1 wherein R<sub>2</sub> is CH<sub>2</sub>CH<sub>3</sub>, CH<sub>3</sub>, CF<sub>2</sub>H, CH<sub>2</sub>-cyclopropyl, or cyclopentyl.
11. The compound of claim 1 wherein R<sub>6</sub> and R<sub>7</sub> are both H or one of R<sub>6</sub> and R<sub>7</sub> is H and the other is CH<sub>3</sub>.
- 20
12. The compound of claim 1 wherein X<sub>4</sub> is -NHC(O)R<sub>8</sub> and X<sub>1</sub> is H or halogen.
13. The compound of claim 1 wherein one of X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, and X<sub>4</sub> is NHCOCH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, NHCON(CH<sub>3</sub>)<sub>2</sub>, NHCONH<sub>2</sub>, NHCOCH<sub>3</sub>, NHCOCH(R<sub>8</sub>)N(R<sub>7</sub>R<sub>8</sub>) or OCH<sub>3</sub>, and the rest of X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, and X<sub>4</sub> are H.
- 25
14. The compound of claim 1, wherein the configuration of stereocenter a is (S).
- 30
15. The compound of claim 1, wherein the configuration of stereocenter a is (R).

16. The compound of claim 1, wherein R<sub>6</sub> and R<sub>7</sub> are not same, and the configuration of stereocenter **b** is (S).

17. The compound of claim 1, wherein R<sub>6</sub> and R<sub>7</sub> are not same, and the configuration of stereocenter **b** is (R).

18. A diastereomerically pure SS isomer of a compound of claim 1, substantially free of other diasteriomers, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof.

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19. A diastereomerically pure RS isomer of a compound of claim 1, substantially free of other diasteriomers, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof.

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20. A diastereomerically pure SR isomer of a compound of claim 1, substantially free of other diasteriomers, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof.

21. A diastereomerically pure RR isomer of a compound of claim 1, substantially free of other diasteriomers, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof.

22. A compound, where the compound is:

(3R)-(tert-Butoxy)-N-{3-[7-(cyclopropylcarbonylamino)-1-oxoisindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl}carbonylamino (tert-butoxy)formate;  
N-[3-(7-Amino-1-oxoisindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl](tert-butoxy)carbonylamino (tert-butoxy)formate;  
(1R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-3-(N-formyl-N-hydroxy-amino)-propyl]-3-oxo-2,3-dihydro-1H-isooindol-4-yl}-amide;  
(1R)-N-{2-[1-(3-Ethoxy-4-methoxy-phenyl)-3-(N-formyl-N-hydroxy-amino)-propyl]-3-oxo-2,3-dihydro-1H-isooindol-4-yl}-acetamide;  
(1R)-N-{2-[1-(3-Ethoxy-4-methoxy-phenyl)-3-(N-formyl-N-hydroxy-amino)-propyl]-3-oxo-2,3-dihydro-1H-isooindol-4-yl}-isobutyramide;

(1R)-N-{2-[1-(3-Ethoxy-4-methoxy-phenyl)-3-(N-formyl-N-hydroxy-amino)-propyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-4-yl}-acetamide;

(1R)-N-{2-[3-(N-Acetoxy-N-formyl-amino)-1-(3-ethoxy-4-methoxy-phenyl)-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-isobutyramide;

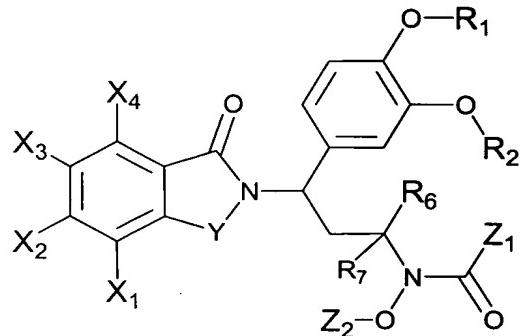
(1R)-N-{2-[3-(N-Aminocarbonyl-N-hydroxy-amino)-1-(3-ethoxy-4-methoxy-phenyl)-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-isobutyramide;

(1R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-3-(N-formyl-N-hydroxy-amino)-propyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide;

(N-{3-[7-(Cyclopropylcarbonylamino)-1-oxoisindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl}acetylamino) acetate; or

(1R)-Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-3-(formyl-hydroxy-amino)-butyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide.

23. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, excipient, or diluent and a compound of formula (I):



5 wherein:

Y is -C(O)-, -CH<sub>2</sub>-, -CH<sub>2</sub>C(O)-or -SO<sub>2</sub>-;

R<sub>1</sub> and R<sub>2</sub> are each independently C<sub>1-8</sub>-alkyl, CF<sub>2</sub>H, CF<sub>3</sub>, CH<sub>2</sub>CHF<sub>2</sub>, cycloalkyl, or (C<sub>1-8</sub>-alkyl)cycloalkyl;

Z<sub>1</sub> is H, C<sub>1-6</sub>-alkyl, NH<sub>2</sub>, NR<sub>3</sub>R<sub>4</sub> or OR<sub>5</sub>;

10 Z<sub>2</sub> is H or C(O)R<sub>5</sub>;

X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub> and X<sub>4</sub> are each independently H, halogen, NO<sub>2</sub>, OR<sub>3</sub>, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl, (C<sub>0-4</sub>-alkyl)-(C<sub>3-6</sub>-cycloalkyl), (C<sub>0-4</sub>-alkyl)-N-(R<sub>8</sub>R<sub>9</sub>), (C<sub>0-4</sub>-alkyl)-NHC(O)-(R<sub>8</sub>), (C<sub>0-4</sub>-alkyl)-NHC(O)CH(R<sub>8</sub>)(R<sub>9</sub>), (C<sub>0-4</sub>-alkyl)-NHC(O)N(R<sub>8</sub>R<sub>9</sub>), (C<sub>0-4</sub>-alkyl)-NHC(O)O(R<sub>8</sub>), (C<sub>0-4</sub>-alkyl)-O-R<sub>8</sub>, (C<sub>0-4</sub>-alkyl)-imidazolyl, (C<sub>0-4</sub>-alkyl)-pyrrolyl, (C<sub>0-4</sub>-alkyl)-

15 oxadiazolyl, (C<sub>0-4</sub>-alkyl)-triazolyl or (C<sub>0-4</sub>-alkyl)-heterocycle;

$R_3$ ,  $R_4$ , and  $R_5$  are each independently H, C<sub>1-6</sub>-alkyl, O-C<sub>1-6</sub>-alkyl, phenyl, benzyl, or aryl;

$R_6$  and  $R_7$  are independently H or C<sub>1-6</sub>-alkyl;

$R_8$  and  $R_9$  are each independently H, C<sub>1-9</sub>-alkyl, C<sub>3-6</sub>-cycloalkyl, (C<sub>1-6</sub>-alkyl)-(C<sub>3-6</sub>-

5 cycloalkyl), (C<sub>0-6</sub>-alkyl)-N( $R_4R_5$ ), (C<sub>1-6</sub>-alkyl)-OR<sub>5</sub>, phenyl, benzyl, aryl, piperidinyl, piperizinyl, pyrrolidinyl, morpholino, or C<sub>3-7</sub>-heterocycloalkyl; or a pharmaceutically acceptable salt or solvate thereof.

24. The pharmaceutical composition of claim 23 further comprising an  
10 additional therapeutic agent.

25. The pharmaceutical composition of claim 24 wherein the additional therapeutic agent is an anti-cancer agent or an anti-inflammatory agent.

15 26. The pharmaceutical composition of claim 25 wherein the anti-cancer agent is paclitaxel, cisplatin, tamoxifen, docetaxel, pirubicin, doxorubicin, irinotecan, leuprolide, bicalutamide, a goserlin implant, gemcitabine, sargramostim or a steroid.

27. A method of inhibiting PDE4 in a mammal comprising administering  
20 to said mammal an effective amount of a compound of claim 1.

25 28. A method of modulating the production of TNF- $\alpha$  in a mammal comprising administering to said mammal an effective amount of a compound of claim 1.

29. A method of inhibiting MMP in a mammal comprising administering to said mammal an effective amount of a compound of claim 1.

30 30. A method of treating, preventing or managing Myelodysplastic Syndrome which comprises administering to a patient in need of such treatment, prevention or management a therapeutically or prophylactically effective amount of a compound of claim 1.

31. A method of treating, preventing or managing Myeloproliferative Disease which comprises administering to a patient in need of such treatment, prevention or management a therapeutically or prophylactically effective amount of a compound of claim 1.

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32. A method of treating, preventing or managing Parkinson's Disease, which comprises administering to a patient in need of such treatment, prevention or management a therapeutically or prophylactically effective amount a compound of claim 1.

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33. A method of treating, preventing or managing complex regional pain syndrome, which comprises administering to a patient in need of such treatment, prevention or management a therapeutically or prophylactically effective amount a compound of claim 1.

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34. The method of claim 31 wherein the therapeutically or pharmaceutically effective amount of a compound of claim 1 is administered before, during or after surgery or physical therapy directed at reducing or avoiding a symptom of complex regional pain syndrome in the patient.

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35. A method of treating, preventing or managing undesired angiogenesis which comprises administering to a patient in need of such treatment, prevention or management a therapeutically effective amount of a compound of claim 1.

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36. A method of treating, preventing or managing cancer which comprises administering to a patient in need of such treatment, prevention or management a therapeutically effective amount of a compound of claim 1.

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37. The method of claim 36 wherein the cancer is a solid tumor or a blood-born tumor.

38. The method of claim 37 wherein the cancer is of the skin; lymph node; breast; cervix; uterus; gastrointestinal tract; lung; ovary; prostate; colon; rectal;

mouth; brain; head and neck; throat; testes; kidney; pancreas; bone; spleen; liver; bladder; larynx; or nasal passages.

39. A method of treating, preventing or managing a disease which  
5 comprises administering to a patient in need of such treatment, prevention or  
management an effective amount of a compound of claim 1, wherein the disease is an  
inflammatory disease, autoimmune disease, arthritis, rheumatoid arthritis,  
inflammatory bowel disease, Crohn's disease, aphthous ulcers, cachexia, graft versus  
host disease, asthma, adult respiratory distress syndrome, or acquired immune  
10 deficiency syndrome.

40. A method of treating, preventing or managing inflammation of the  
lungs which comprises administering to a patient in need of such treatment,  
prevention or management an effective amount of a compound of claim 1.

15 41. A method of treating, preventing or managing depression which  
comprises administering to a patient in need of such treatment, prevention or  
management an effective amount of a compound of claim 1.

20 42. A method of treating, preventing or managing chronic obstructive  
pulmonary disorder which comprises administering to a patient in need of such  
treatment, prevention or management an effective amount of a compound of claim 1.

25 43. The method of claim 42 wherein the compound is administered via an  
inhaler.

44. A method of treating, preventing or managing inflammatory bowel  
disease which comprises administering to a patient in need of such treatment,  
prevention or management an effective amount of a compound of claim 1.

30 45. A method of treating, preventing or managing atopic dermatitis which  
comprises administering to a patient in need of such treatment, prevention or  
management an effective amount of a compound of claim 1.

46. A method of treating, preventing or managing psoriasis which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1.

5 47. The method of claim 46 wherein the compound is administered topically

10 48. A method of treating, preventing or managing Crohn's disease which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1.

15 49. A method of treating, preventing or managing rheumatoid arthritis which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1.

50. A method of treating, preventing or managing asthma which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1.

20 51. The method of claim 50, wherein the compound is administered via an inhaler.

25 52. A method of treating, preventing or managing multiple sclerosis which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1.

53. A method of treating, preventing or managing heart disease which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1.

30 54. A method of treating, preventing or managing macular degeneration which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1.

55. A method of treating, preventing or managing a central nervous system disorder which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1.

5 56. A method of treating, preventing or managing an asbestos-related disease or disorder which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a compound of claim 1.

10 57. The method of any one of claims 27-56 wherein the patient, mammal or mammalian cell is human.